



6-28-04

JFW

AM-101251

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No. : 10/810,517 Confirmation No.: 1212
Applicant : Kreft et al.
Filed : March 26, 2004
TC/A.U. : 1626
Examiner : unassigned
Customer No. : 38199
Title : FLUORO- AND TRIFLUOROALKYL-CONTAINING
HETEROCYCLIC SULFONAMIDE INHIBITORS OF BETA-
AMYLOID PRODUCTION AND DERIVATIVES THEREOF

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Sir:

Applicants submit to the Examiner the attached Form PTO/SB/08A/B document listing and this paper pursuant to 37 CFR § 1.56 and § 1.97-1.98. Form PTO/SB/08A/B is attached and copies of the documents are enclosed herewith. This Information Disclosure Statement is submitted less than three months from the filing date of this application and before the receipt of a first Office Action on the merits. Therefore, no fees are believed due.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Express Mail No. EU531571505US

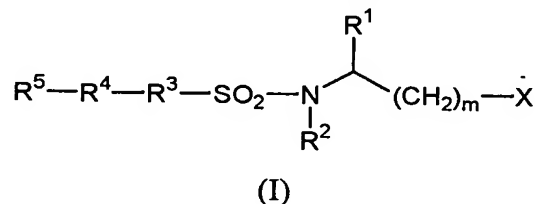
REMARKS

Listed below are previously filed, and co-pending, US Patent applications.

- (i) US Provisional Patent Application No. 60/255,105, filed December 13, 2000 (now abandoned)
- (ii) US Patent Application No. 10/014,304, filed December 11, 2001, now US Patent No. 6,610,734, issued August 26, 2003 (item BC)
International Patent Application No. PCT/US01/48375, published as International Patent Publication No. WO 02/057252 on July 25, 2002 (item CP)
- (iii) US Patent Application No. 10/166,896, filed June 11, 2002, now US Patent No. 6,657,070, issued December 2, 2003 (item BB)
International Patent Application No. PCT/US02/38117, published as International Patent Publication No. WO 03/050062 on June 19, 2003 (item DM)
- (iv) US Patent Application No. 10/455,674, filed June 5, 2003
(US Patent Publication No. US-20030229127-A1, published December 11, 2003 (item BD))
- (v) US Provisional Patent Application No. 60/387,690, filed June 11, 2002 (now abandoned)
- (vi) US Patent Application No. 10/457,641, filed June 9, 2003
(US Patent Publication No. US-20040006050-A1, published January 8, 2004 (item BF))
International Patent Application No. PCT/US03/18198, published as International Patent Publication No. WO 03/103660-A1 on December 18, 2003 (item DL)
- (vii) US Provisional Patent Application No. 60/339,264, filed December 11, 2001 (now abandoned)
- (viii) US Patent Application No. 10/304,322, filed November 26, 2003
(US Patent Publication No. 20030144531-A1, published July 31, 2003 (item BE))
International Patent Application No. PCT/US02/38119, published as International Patent Publication No. WO 03/050063 on June 19, 2003 (item CQ)

An English translation of document BO was not available. Applicants have therefore provided a copy of an English language abstract as document DL and the following remarks:

This document describes sulfonamide derivatives of the following structure (I):



where: R^1 = lower alkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl (all optionally substituted), COR^6 , or $-\text{NHCO}-(\text{CH}_2)_x-\text{R}^{26}$;

R^2 = H, lower alkyl, $-(\text{CH}_2)_t-\text{O}-\text{R}^{27}$ or aralkyl

R^3 = optionally substituted arylene or heteroarylene, or a single bond;

R^4 = $-(\text{CH}_2)_n-$, $-\text{CH}=\text{CH}-$, $-\text{C}\equiv\text{C}-$, $-\text{CO}-$, $-\text{CO}-\text{NH}-$, $-\text{N}=\text{N}-$, $-(\text{R}')-$, $-\text{NH}-\text{CO}-\text{NH}-$, $-\text{NH}-\text{CO}-$, $-\text{O}-$, $-\text{S}-$, $-\text{SO}_2\text{NH}-$, $-\text{SO}_2-\text{NH}-\text{N}=\text{CH}-$, tetrazolediyl, piperazinediyl, piperidinediyl, or a single bond;

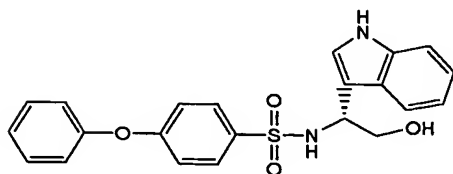
R^5 = optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkyl, aralkyl, aralkyloxy, non-aromatic heterocyclic, or lower alkyloxycarbonyl (lower alkenyl);

X = $-\text{SR}^7$, $-\text{OR}^8$, $-\text{SCOR}^9$, $-\text{OCOR}^{10}$, $-\text{XCO}^2\text{R}^{25}$, or $-\text{SCONHR}^{11}$; and

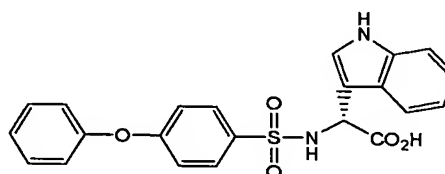
$m = 1$ or 2 ;

wherein R^1 is not CH_3 or aminocarbonyl when R^3 and R^4 are single bonds and R^5 is optionally substituted aryl or heteroaryl.

This document also describes the following specific compounds (II) and (III):



(II)



(III)

The compounds of item BO are assertedly useful as $\text{TNF-}\alpha$ inhibitors, treating autoimmune diseases such as chronic rheumatism, Crohn's disease, myasthenia gravis, systemic lupus erythematosus, asthma, diabetes type I, and psoriasis.

The months of publication for documents AR-AT, AX, BU-BW, CS, CV, and CY-CZ could not be determined. The years of publication for documents AR-AT, AZ, BU-BW, CS, and CY-CZ are sufficiently earlier than the effective US filing date and/or the foreign priority date of the present application so that the particular months of publication of these documents is not in issue (MPEP 609).

The Examiner is respectfully requested to consider the enclosed documents identified in this paper and in the attached Form PTO/SB/08A/B during the course of examination of this application.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

HOWSON AND HOWSON
Attorneys for Applicants

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**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

| | | |
|---|-----------------------------|----------------|
| Application Number | 10/810,517 | |
| | Filing Date | March 26, 2004 |
| | First Named Inventor | Kreft et al. |
| | Art Unit | 1626 |
| | Examiner Name | unassigned |
| Attorney Docket Number | AM-101251 | |
| Total Number of Pages in This Submission | 11 | |

ENCLOSURES (Check all that apply)

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| <input type="checkbox"/> Fee Transmittal Form | <input type="checkbox"/> Drawing(s) | <input type="checkbox"/> After Allowance communication to Technology Center (TC) |
| <input type="checkbox"/> Fee Attached | <input type="checkbox"/> Licensing-related Papers | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences |
| <input type="checkbox"/> Amendment/Reply | <input type="checkbox"/> Petition | <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) |
| <input type="checkbox"/> After Final | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Proprietary Information |
| <input type="checkbox"/> Affidavits/declaration(s) | <input type="checkbox"/> Power of Attorney, Revocation | <input type="checkbox"/> Status Letter |
| <input type="checkbox"/> Extension of Time Request | <input type="checkbox"/> Change of Correspondence Address | <input type="checkbox"/> Other Enclosure(s) (please identify below): |
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| <input type="checkbox"/> Response to Missing Parts/Incomplete Application | Remarks | |
| <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | Customer No. 38199 Express Mail No. EU531571505US | |

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | |
|--------------------------------|---------------------------------------|
| Firm or Individual name | HOWSON AND HOWSON Cathy A. Kodroff |
| Signature | |
| Date | June 25, 2004 |

CERTIFICATE OF TRANSMISSION/MAILING

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PTO/SB/08A (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
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| | | | | Application Number | 10/810,517 |
| | | | | Filing Date | March 26, 2004 |
| | | | | First Named Inventor | Kreft et al. |
| | | | | Group Art Unit | 1626 |
| | | | | Examiner Name | unassigned |
| Sheet | 1 | of | 6 | Attorney Docket Number | AM-101251 |

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|-----------------------|--|--------------------------------|---|---|
| Examiner Initials* | Cite No. ¹ | Document Number | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number-Kind Code ² (if known) | | | |
| | AA | US-5,981,168 | P. Reiner | 11-09-1999 | |
| | AB | US-5,624,937 | J. Reel | 04-29-1997 | |
| | AC | US-5,703,129 | K. Felsenstein | 12-30-1997 | |
| | AD | US-5,593,846 | D. Schenk | 01-14-1997 | |
| | AE | US-5,852,007 | S. Chatterjee | 12-22-1998 | |
| | AF | US-6,248,775 | Vasquez | 06-19-2001 | |
| | AG | US-6,376,523 | Chan, et al. | 04-23-2002 | |
| | AH | US-5,594,021 | Chan, et al. | 01-14-1997 | Claims 1 and 2, and Specification |

| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|-----------------------|--|--------------------------------|---|---|----------------|
| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | Country Code ³ - Number ⁴ -Kind Code ⁵ (if known) | | | | |
| | AL | WO-95/29904-A1 | 11-09-1995 | K. Chow | | |
| | AM | WO-98/03166-A1 | 01-29-1998 | G. DeCrescenzo | | |
| | AN | WO-98/22104-A3 | 05-28-1998 | G. Pasinetti | | |
| | AO | WO-98/22493-A2 | 05-28-1998 | J. Audia | | |
| | AP | WO-00/09107-A2 | 02-24-2000 | D. Ross | | |
| | AQ | WO-00/50391-A1 | 08-31-2000 | D. Smith | | |

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| | | | | Group Art Unit | 1626 |
| | | | | Examiner Name | unassigned |
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U.S. PATENT DOCUMENTS

| Examiner Initials* | Cite No. ¹ | Document Number | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|-----------------------|--|--------------------------------|---|---|
| | | Number-Kind Code ² (if known) | | | |
| | AI | US-5,571,821 | Chan, et al. | 11-05-1996 | |
| | AJ | US-5,464,853 | Chan, et al. | 01-07-1997 | |
| | AK | US-5,591,761 | Chan, et al. | 05-07-1996 | |
| | BA | US-5,514,691 | Chan, et al. | 11-07-1995 | |

FOREIGN PATENT DOCUMENTS

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|--------------------|-----------------------|--|--------------------------------|---|---|----------------|
| | | Country Code ³ - Number ⁴ -Kind Code ⁵ (if known) | | | | |
| | BL | EP-652,009 | 05-10-1995 | V. John | | |
| | BM | EP-510,700-A2 | 10-28-1992 | K. Itoh et al. | | |
| | BN | EP-1,172,361-A1 | 12-14-1999 | Watanabe et al. | | |
| | BO | JP-5-148233 | 06-15-1993 | Y. Ito | | √ |
| | BP | JP-11-343279 | 01-16-2002 | F. Watanabe | | |
| | BQ | WO-01/27091-A1 | 04-19-2001 | Thompson | | |
| | CL | WO-01/27108-A1 | 04-19-2001 | Thompson | | |
| | CM | WO-01/23379-A1 | 04-05-2001 | Arkinstall et al. | | |
| | CN | EP-1,088,821-A1 | 04-04-2001 | Arkinstall | | |

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| Examiner Signature | | Date Considered | |
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| | | | | Examiner Name | unassigned |
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| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|-----------------------|--|--------------------------------|---|---|
| Examiner Initials* | Cite No. ¹ | Document Number | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number-Kind Code ² (if known) | | | |
| | BB | US-6,657,070 | 12-02-2003 | Resnick, et al. | |
| | BC | US-6,610,734 | 08-26-2003 | Kreft, et al. | |
| | BD | US-20030229127-A1 | 12-11-2003 | Kreft, et al. | |
| | BE | US-20030144531-A1 | 07-31-2003 | Kreft, et al. | |
| | BF | US-20040006050-A1 | 01-08-2004 | Kreft, et al. | |
| | BG | 6,566,536 | 05-20-2003 | Muller, et al. | |
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| FOREIGN PATENT DOCUMENTS | | | | | | |
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| | | Country Code ³ - Number ⁴ -Kind Code ⁵ (if known) | | | | |
| | CO | WO-01/70677-A1 | 09-27-2001 | Belanger et al. | | |
| | CP | WO-02/057252-A1 | 07-25-2002 | Kreft et al. | | |
| | CQ | WO-03/050063-A1 | 06-19-2003 | Kreft et al. | | |
| | DL | WO-03/103660-A1 | 12-18-2003 | Kreft et al. | | |
| | DM | WO-03/050062-A1 | 06-19-2003 | Resnick et al. | | |
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| | | | | Examiner Name | unassigned |
| Sheet | 4 | of | 6 | Attorney Docket Number | AM-101251 |

NONPATENT LITERATURE DOCUMENTS

| Examiner Initials* | Cite No. ¹ | Include the name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item, (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T ² |
|-----------------------|--------------------------|---|----------------|
| | AR | A. LARNER et al, "Review - Central & Peripheral Nervous Systems - Alzheimer's Disease: Towards Therapeutic Manipulation of the Amyloid Precursor Protein and Amyloid β -peptides", Exp. Opin. Ther. Patents, 7(10):1115-1127 (1997) | |
| | AS | C. MOORE et al, "Inhibition of β -amyloid Formation as a Therapeutic Strategy", Exp. Opin. Ther. Patents, 9(2):135-146 (1999) | |
| | AT | V. JOHN et al, "Alzheimer's Disease: Recent Advances on the Amyloid Hypothesis", in Annual Reports in Medicinal Chemistry, Chapter 2, pp. 11-20 (1997) | |
| | AU | G. RISHTON et al, "Fenchylamine Sulfonamide Inhibitors of Amyloid β Peptide Production by the γ -Secretase Proteolytic Pathway: Potential Small-Molecule Therapeutic Agents for the Treatment of Alzheimer's Disease", J. Med. Chem., 43(12):2297-2299 (June 15, 2000) | |
| | AV | B. TESTA et al, "Prodrugs Revisited: The "Ad Hoc" Approach as a Complement to Ligand Design", Medicinal Research Reviews, 16(3):233-241 (May, 1996) | |
| | AW | D. SKOVRONSKY et al, " β -Secretase Revealed: Starting Gate for Race to Novel Therapies for Alzheimer's Disease", TIPS, 21:161-163 (May, 2000) | |
| | AX | A. GHOSH et al, "Design of Potent Inhibitors for Human Brain Memapsin 2 (β -Secretase)", J. Am. Chem. Soc., 122:3522-3523 (2000) | |
| | AY | W. ESLER et al, "Transition-State Analogue Inhibitors of γ -Secretase Bind Directly to Presenilin-1", Nature Cell Biology, 2:428-434 (July, 2000) | |
| | AZ | Y-M. LI et al, "Photoactivated γ -Secretase Inhibitors Directed to the Active Site Covalently Label Presenilin 1", Nature, 405:689-694 (June, 2000) | |
| | BR | M. WOLFE et al, "A Substrate-Based Difluoro Ketone Selectively Inhibits Alzheimer's β -Secretase Activity", J. Med. Chem., 41:6-9 (January 1, 1998) | |

| | | | |
|-----------------------|--|--------------------|--|
| Examiner Signature | | Date Considered | |
|-----------------------|--|--------------------|--|

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¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 USC 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETE FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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| | | | | Application Number | 10/810,517 |
| | | | | Filing Date | March 26, 2004 |
| | | | | First Named Inventor | Kreft et al. |
| | | | | Group Art Unit | 1626 |
| | | | | Examiner Name | unassigned |
| | | | | Attorney Docket Number | AM-101251 |
| Sheet | 5 | of | 6 | | |

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| Examiner Initials* | Cite No. ¹ | Include the name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item, (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published | T ² |
|-----------------------|--------------------------|---|----------------|
| | BS | S. SINHA et al, "Purification and Cloning of Amyloid Precursor Protein β -Secretase from Human Brain", Nature, 402:537-540 (December, 1999) | |
| | BT | A. GOATE, "Monogenetic Determinants of Alzheimer's Disease: APP Mutations", CMLS Cell. Mol. Life Sci., 54:897-901 (September, 1998) | |
| | BU | M. SABBAGH et al, " β -Amyloid and Treatment Opportunities for Alzheimer's Disease", Alzheimer's Disease Review, 3:1-19 (1997) | |
| | BV | C. AUGELLI-SZAFRAN et al, " β -Amyloid as a Target for Alzheimer's Disease Therapy, in Annual Reports in Medicinal Chemistry, Chapter 3, pp. 21-30 (1999) | |
| | BW | J-C. DODART et al, "The β -Amyloid Precursor Protein and its Derivatives: from Biology to Learning and Memory Processes", Reviews in the Neurosciences, 11(2-3):75-93 (2000) | |
| | BX | D. SMALL et al, "Alzheimer's Disease and the Amyloid β Protein: What is the Role of Amyloid?", Journal of Neurochemistry, 73(2):443-449 (August, 1999) | |
| | BY | J. NÄSLUND et al, "Correlation Between Elevated Levels of Amyloid β -Peptide in the Brain and Cognitive Decline", JAMA, 283(12):1571-1577 (March, 2000) | |
| | BZ | Q-X. LI et al, "The Amyloid Precursor Protein of Alzheimer Disease in Human Brain and Blood", Journal of Leukocyte Biology, 66:567-574 (October, 1999) | |
| | CR | S. WAGNER et al, "Modulation of Amyloid β Protein Precursor Processing as a Means of Retarding Progression of Alzheimer's Disease", The Journal of Clinical Investigation, 104(10):1329-1332 (November, 1999) | |
| | CS | Y. HAN et al, "Total Asymmetric Synthesis of Highly Constrained Amino Acids Isopropyl-2', 6'-Dimethyl-Tyrosines", Tetrahedron Letters, 38(29):5135-5138 (1997) | |
| | CT | M. FINDEIS et al, "Modified-Peptide Inhibitors of Amyloid β -Peptide Polymerization", Biochemistry, 38(21):6791-6800 (May, 1999) | |

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|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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|--------------------|-----------------------|---|----------------|
| | CU | ROGGO, "Inhibition of BACE, A Promising Approach to Alzheimer's Disease Therapy", Curr. Top. Med. Chem., 2(4): 359-70 (April 2002) | |
| | CV | TUNG et al., "Design of Substrate-Based Inhibitors of Human β -Secretase", J. Med. Chem., 45(2):259-262 (2002) | |
| | CW | JOSIEN, "Recent Advances in the Development of Gamma-Secretase Inhibitors", Curr. Opin. Drug. Discov. Devel., 5(4):513-25 (July 2002) | |
| | CX | DOVEY et al., "Functional Gamma-Secretase Inhibitors Reduce Beta-Amyloid Peptide Levels in Brain", J. Neurochem., 76:173-181 (January 2001) | |
| | CY | OLSON et al., "Chapter 4. Secretase Inhibitors as Therapeutics for Alzheimer's Disease", Ann. Reports in Med. Chem., 35:31 (2000) | |
| | CZ | VARGHESE et al., "Chapter 2. Alzheimer's Disease: Recent Advances on the Amyloid Hypothesis", Ann. Reports Med. Chem., 32:11 (1997) | |
| | DL | Abstract of Japanese Patent No. JP-11-343279, January 26, 2002 | |
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